Applicants have used alternative terms "contiguous" and "consecutive"simply for clarity. Although, the need to distinguish the portion of the RRF that comprises the consecutive amino acid residues from the consecutive amino acids themselves is unnecessary for Claim 69, as the Examiner appears to be stating, this distinction helps to clarify the meaning of dependent Claim 78.

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 second paragraph are respectfully solicited.

The Specification Enables Any Person Skilled in the Art to Make and Use the Invention

The Examiner has rejected Claims 1 and 69-96 as containing subject matter which was not disclosed in the Specification in such a way as to enable the skilled artisan to use the invention. The Examiner asserts that the Specification only provides properties for the ISGF-3 that are useful for basic research and provides no guidance as to how these characteristics are put to a practical use. The Examiner also asserts that there is no guidance as to how one could treat a disease correlated with ISGF activity without causing harmful side effects. The Examiner further asserts that the skilled artisan would not believe that gene inhibition would lead to a diseased treatment without further guidance as to how one could inhibit the gene activity in the diseased cells without harming the same activity in normal cells.

The Applicants respectfully traverse the Examiner's rejections. The Applicants have amended Claims 1, 69, and 78 and added additional Claims 97-109 so as to more distinctly claim and particularly point out the subject matter of their invention. However, the Applicants respectfully disagree with the Examiner's assertion that the Specification must provide guidance for treating a disease without causing harmful side effects, in order to enable a skilled artisan to make and use the claimed receptor recognition factors and the nucleic acids that encode them.

Indeed, the instant Specification fully enables the skilled artisan to make and use the claimed proteins and nucleic acids. Furthermore, the instant Specification teaches that the receptor recognition factors are involved in signal transduction and play important biological

roles. In recent years, these biological roles have been even further elucidated. Thus, it is now known that the claimed receptor recognition factors are a family of proteins that comprises only seven members "that are activated by virtually every cytokine and growth factor." [Bromberg, *Breast Cancer Res.* **2**:86-90 (2000), Abstract enclosed in Exhibit 1]. Furthermore, Ivashkiv [*Rev. Immunogenet.*, 2:220-230 (2000), Abstract enclosed in Exhibit 1] has stated that:

> "STATs play critical, nonredundant roles in mediating cellular transcriptional responses to cytokines, and in cell activation, survival, and proliferation."

More specifically, Stat 3 has been implicated in cardiac remodeling [Yamauchi-Takihara and Kishimoto, *Trends Cardiovasc Med.* **10**:298-303 (2000)Abstract enclosed in Exhibit 1] and and in the clonal stem cell disorder known as polycythemia vera [Roder *et al.*, *Exp. Hematol.* **29**:694-702 (2001)Abstract enclosed in Exhibit 1]. Furthermore, Shen *et al.* have shown that Stat3 can protect cells against apoptosis [*ProcNat.Acad.Sci.*, **98**:1543-1548 (2001)]. Therefore, STAT proteins indeed play an important biological role.

Accordingly, the claimed receptor recognition factors and the nucleic acids that encode them have important practical uses. For example, the instant Specification teaches the use of antibodies to the claimed receptor recognition factors in diagnostics (*see* Page 39, lines 22-26 of the instant Specification) and the use of the nucleic acids in the isolation of additional family members (*see* Example 4 of the instant Specification). It has been stated that for STATs the "critical role in development and normal cell signaling has been largely determined through the analysis of transgenic mice lacking individual STAT genes," [Bromberg, (2000) *supra,* Abstract] and indeed, it is the teachings of the instant Specification that enables the construction of such transgenic mice.

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112 first paragraph are respectfully solicited.

From the above and foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is earnestly solicited.

Attached hereto is a marked up version of the changes made to the Specification and claims by the current amendment. The attached page is captioned "Version with marking to show changes made."

No additional fees are believed to be necessitated by the foregoing amendments. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

In the event that there are any questions concerning this Amendment, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

Michael D. Davis

MICHAEL D. DAVIS
Attorney for Applicant(s)
Registration No. 39,161

KLAUBER & JACKSON
411 Hackensack Avenue
Hackensack, New Jersey 07601
(201) 487-5800
Date: June 15, 2001

"VERSION WITH MARKING TO SHOW CHANGES MADE."

IN THE SPECIFICATION:

The title of the application has also been amended to read:

~~NUCLEIC ACIDS ENCODING~~ RECEPTOR RECOGNITION FACTORS, AND METHODS OF USE THEREOF

IN THE CLAIMS:

The Claims 1, 69, and 78 have been amended as follows:

1. (Amended) An isolated receptor recognition factor (RRF) implicated in the transcriptional stimulation of genes in target cells in response to the binding of a specific polypeptide ligand to its cellular receptor on said target cell, wherein said receptor recognition factor ~~having the following characteristics:~~

~~a) apparent direct interaction with the ligand-bound receptor and activation of one or more transcription factors capable of binding with a specific gene;~~

~~b) an activity demonstrably unaffected by the presence or concentration of second messengers;~~

~~c) direct interaction with tyrosine kinase domains; and~~

~~d) a perceived an absence of interaction with G-proteins~~ is a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, and SEQ ID NO:12.

69. (Amended) A recombinant DNA molecule encoding a receptor recognition factor (RRF) protein having the following characteristics:

a) said RRF is cytoplasmic in origin;

b) said RRF is activated by tyrosine phosphorylation;

c) upon activation said RRF is translocated to the nucleus of a target cell; and

d) said RRF has an amino acid sequence comprising a sequence of contiguous amino acid residues that contains four or more consecutive amino acids which ~~is~~ are present in both SEQ ID NO:2 and SEQ ID NO:4~~; wherein the sequence of contiguous amino acid residues contains four or more consecutive amino acids~~.

78. (Amended) The recombinant DNA molecule of Claim 70 wherein said RRF has an amino acid sequence which further comprises a second sequence of contiguous amino acid residues that ~~, wherein the second sequence of contiguous amino acid residues~~ also contains four or more consecutive amino acids which ~~is~~ are present in both SEQ ID NO:2 and SEQ ID NO:4.

Claims 97-109 have been added.